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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/516,613	12/03/2004	Paolo Alberto Veronesi	IPU1954-008	7113

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EXAMINER	
AUDET, MAURY A	
ART UNIT	PAPER NUMBER
1654	

MAIL DATE	DELIVERY MODE
02/05/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/516,613	VERONESI ET AL.	
	Examiner	Art Unit	
	MAURY AUDET	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *9/27/07*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19 and 34-41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19 and 34-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

As noted before, the present application has been transferred from Examiner Harle to the present Examiner.

Invention

Applicant's invention is now to methods of making/using nasal compositions comprising THAM (also known as [tris(hydroxymethyl)aminomethane] or TRIS or tromethamine) with any nasally administrable peptide (and other random additives commonly used in like-kind compositions). It was noted that the European International Authority had cited 3 "X" references (EP 0726075A; WO0152937 (now US 6,434,162); and IT 1243742) as expressly teaching all originally filed 24 claims. It is noted that Applicant has since amended the claims (the Examiner finds only as to the amount of THAM administered), in an attempt to get around 1 or more of these references cited by the International Authority. The amount of THAM originally filed throughout claims was any amount or any amount between 0.5 mg/ml to 30 mg/ml. The amount of THAM now amended claimed into e.g. claims 11-12, 26, 30-31, and 32-34 is "above 4.0 mg/ml to 30 mg/ml" or ranges therein.

It is noted that Applicant's use of the modifier "depolarizing" nasal epithelial cells is merely an inherent physiological property/effect of any composition comprising THAM and a peptide which is or can be administered via the nasal route.

Claim Rejections - 35 USC § 102/103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

The rejection of claims 19 and 34-41 under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Veronesi et al. (EP 0726075A) is maintained for the reasons of record. Applicant's arguments and amendments have been considered but are not found persuasive. The claims have now been amended solely to methods of making/using THAM/tromethamine, asserted to now carry out an unexpected effect of enhancing nasal permeation/bioavailability of any nasal peptide. This is an inherent property, and contrary to Applicant's assertion/arguments that THAM or tromethamine is only a buffer, the art is well-versed that THAM/tromethamine is a permeation enhancer. See merely by example, and by title alone (no reference provided or needed): El Sayed GM. Role of tromethamine as a dissolution and bioavailability enhancer of oral glibenclamide. STP Pharma Sci. 1998;8:169-173. To see a

plethora of other references evidencing this known use/inherent property of THAM/tromethamine, Applicant is directed to simply type the following into even the Non-Patent Literature (PubMed, Yahoo): tromethamine and absorption or permeation. The rejection below stands.

The rejection is repeated below for continuity of record:

Veronesi et al. (Applicant's earlier work to same product) teach a nasally administered composition comprising a nasal peptide (calcitonin) and THAM. Wherein THAM may be administered at from 1.0 to 4.0 mg/ml, as well as the other components of the present invention (entire document, especially abstract, page 2, lines 3-4, claims 1, 4, 5, 7, 8, 11, 15, 16, 23 and Examples 1 and 2). Veronesi et al. does not expressly teach THAM administration of "above 4.0 mg/ml to 30 mg/ml".

As to the 103 side of the amount of THAM/TRIS/tromethamine administration, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to use any known amount of this agent in Veronesi et al. (Applicant's earlier work), because neither Applicants earlier work nor Applicant's the present application - which originally filed claims to any amount of THAM or preferably from 0.5 mg/ml to 30 mg/ml – recite any unexpected result from any amount/range of THAM, thus any known range/amount is deemed to carry out the same effect, absent credible evidence to the contrary. Furthermore, it is noted that another of the cited references (now US 6,434,162) by the same International Authority discussed above, recites the use of about 1.5 mg/ml to about 4.5 mg/ml – e.g. "above 4.0 mg/ml" – e.g. "above 4.0 mg/ml". So even if Applicant does overcome the New Matter Rejection and

102 rejection, it would have been obvious to one of ordinary skill in the art to use THAM at "above 4.0 mg/ml" for the same purpose/composition].

From the teachings of the reference(s), it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MAURY AUDET whose telephone number is (571)272-0960. The examiner can normally be reached on M-Th. 7AM-5:30PM (10 Hrs.).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MA, 8/2/2008